Foxp1-mediated programming of limb-innervating motor neurons from mouse and human embryonic stem cells.

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Public Summary:
The differentiation of spinal motor neurons (MNs) from mouse and human embryonic stem cells provides opportunities to model MN development and disease, but most protocols produce only a subset of the MN subtypes found in vivo. Here we show that limb projecting lateral motor column MNs can be efficiently generated though the expression of the transcription factor Foxp1. Foxp1-programmed MNs preferentially project axons towards limb muscle in cell culture experiments and distal limb muscles upon transplantation into the developing chick spinal cord.

Scientific Abstract:
Spinal motor neurons (MNs) control diverse motor tasks including respiration, posture and locomotion that are disrupted by neurodegenerative diseases such as amyotrophic lateral sclerosis and spinal muscular atrophy. Methods directing MN differentiation from stem cells have been developed to enable disease modelling in vitro. However, most protocols produce only a limited subset of endogenous MN subtypes. Here we demonstrate that limb-innervating lateral motor column (LMC) MNs can be efficiently generated from mouse and human embryonic stem cells through manipulation of the transcription factor Foxp1. Foxp1-programmed MNs exhibit features of medial and lateral LMC MNs including expression of specific motor pool markers and axon guidance receptors. Importantly, they preferentially project axons towards limb muscle explants in vitro and distal limb muscles in vivo upon transplantation-hallmarks of bona fide LMC MNs. These results present an effective approach for generating specific MN populations from stem cells for studying MN development and disease.